Challenges and Successes in Evaluation and Management of Non-clinical Studies Using a China–based CRO

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Fastest Growing Large Economy in World

– China’s Economy: Grew 25 times in 20 years … Doubled last 5 years

China at Night Seen from Space

Sources: NASA, IMS
CRO Booming in China

- China to become world’s 3rd-largest pharmaceutical market in 2011, 2nd-largest in 2020, and 1st-largest in 2025
- China ranked first among the most favored offshore bases for R&D
- Many expansions and many newcomers in China’s CRO market, ~140 CROs now
- Competition to supply CRO services began to cause consolidation within China

Sources: IMS, UBS, Modular R&D, The CRO Market Outlook
GLP Toxicology Services in China

- Until 2003, there were no GLP regulations, no expertise, and few studies conducted.
- Toxicology CRO industry in China is only a few years old, but ramp up toward standardization and global competitiveness.
- GLP processes are becoming more standardized.
- China’s market for Toxicology services is estimated about $20 million in 2009 and may jump to $200 million in 5 to 7 years.
China’s Toxicology CROs

- Estimated >20 Toxicology CROs in China, varies in size, quality of offerings, and management capabilities
- 9 accredited Toxicology Labs in China so far
- Enthusiasm to learn and work with Western partners, but most local CROs’ customers tend to be local Chinese pharmaceutical companies
- Estimated 2 to 4 million sq. ft. Toxicology facilities are built or under construction in China
Evolving Preclinical Study Capabilities

- FDA and EU regulators’ willingness to accept non-clinical data generated by China-based CROs.

- A number of China-based CROs are close to operating in compliance with Western GLP standards and were audited by FDA and OECD
  - Within 12–24 months, a lot more GLP toxicology studies are expected to be done in China

- China-based CROs
  - The FOREIGN or JOINTLY OWNED CROs: Charles River Lab and WuXi AppTec is leading the way
  - The LOCAL CROs: Pharmaron/Bridge Lab, Joinn Laboratories, and state owned institutions
Conducting Toxicology Studies in China

- **Benefits**
  - Large local talent pool, strong work ethic and eager to learn
  - Access to large non-human primate breeding facilities and offer a clear advantages of conducting non-human primate studies
  - Study cost savings of ~50% and likely to continue within next 5 years

- **Challenges**
  - Due diligence monitoring and managing studies without an in-country presence
  - China's unique regulatory environment and business culture
  - Cultural and language barriers
  - Experienced talent pool is shallow in some areas, particularly at the senior level and well-trained veterinarians and veterinary pathologists from West
China Universities: 5.7 Million Graduates per Year

Sources: National Bureau of Statistics of China
China Labor & Utility Costs: up to 10 times Cheaper than in West

- Labor Cost/Mo: China (4000 USD), US (2000 USD)
- Sewer/m3: China (4000 USD), US (2000 USD)
- Water/m3: China (1000 USD), US (500 USD)
- Electrical/kwh: China (500 USD), US (2000 USD)
Language and Cultural Barriers

- **English skill**
  - English language capabilities are modest at most facilities,
  - Limited pool of English-proficient scientists, technicians, and veterinarians

- **Chinese Culture**
  - FACE (面子): Avoid loss of face, don’t want to admit mistakes or show a lack of knowledge
  - CONNECTIONS (关系，人情): “You scratch my back, I’ll scratch yours”. One is always part of a network and a person’s identity is rarely treated on an individual basis
  - GOLDEN MEAN (中庸): Group orientated, values harmony and stability
Western vs. Chinese Cultures

Hesitant to challenge authority or ask questions
Act based on consensus, rather than on individual initiative

Escape from direct confrontation
Appointment times flexible

Sources: www.yangliudesign.com
Keys to Success – CROs

- **Meet Sponsors’ Expectations**
  - Acceptable lead times, effective process flows, and tracking measures
  - Acceptable documentation and records control procedures
  - Acceptable interim data reporting, error reporting, and ongoing communication
  - Acceptable draft and final report timelines
  - Flexible and Agile: Resource allocation and reallocation procedures to tailor rapidly to specific needs

- **Relationship building**
  - Establish a good working relationship
  - Risk sharing for long-term success

- **Compliance with Western GLP standards**
  - GLP is mindset
  - Quality systems (QC & QA) to ensure international regulatory compliance
  - Management must monitor all aspects of compliance closely on a day-to-day basis

- **Quality of the supply chain**
  - Animals, feed, etc.
Keys to Success for CROs (cont’d)

- Technical proficiency and expertise
  - Establish effective and well-planned training programs
  - Documentation standards: Protocol, SOPs, Reports, Data, and Computer systems
  - “IP through IND” service capabilities

- Establish correction and prevention (vs. punishment) mechanism
  - Employees must strictly adhere to the SOPs in all respects
  - Endeavor to keep errors to a minimum

- Communicate effectively
  - Weekly and ongoing updates/reports with sponsors
  - Constant and consistent communication with employees, focus on clear, open, and honest communication

- Balance between work and everyday life to ensure long-term efficiency
  - Local colleagues can be overly dedicated
  - Retention: Development and growth opportunities and job satisfaction
  - Employees engaged, empowered, committed, and responsible
Keys to Success – Western Sponsors

- Appropriate due diligence and upfront evaluation
  - Scientific Capabilities – Meet your needs
  - GLP Compliance – Quality and GLP practices
  - Preclinical Capacity – Implementation readiness; Experience; Quality of services and quality history; and Process/cycle times
  - Business and Financial Strengths – Financial stability and capabilities of business and technical representatives

- Establish a good working relationship with CROs
  - Turn differences into success, be collaborative and partnership
  - Build relationships, strengthen local connections
  - Adapt China’s unique regulatory environment and business culture

- More supervision and technical support
  - Frequent technical discussions with the CRO staff
  - Pathology peer-review
Study Monitoring

- Establish realistic timelines and expectations
- Consistent monitoring and managing studies
- Communicate effectively
  - With a physical presence in China, is better able to communicate with and supervise work at local CROs
  - Close long-distance oversight – frequent tel/video conferences
- English-speaking monitors and project managers
  - Direct instructions
  - Avoid Western slang
Conclusions

- **The MARKET** – CRO booming in China
- **The STATUS** – A number of CROs in China are close to operating in compliance with Western GLP standards
- **The CULTURES** – Turn Differences into Success
- **The OPPORTUNITIES** – Innovative drug discovery emerging in China and Virtually Integrated Operating Model